

RECEIVED

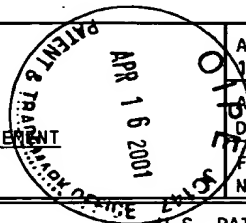
APR 17 2001

TECH CENTER 1600/2900

Page 1 of 9

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe et al.FILING DATE
November 6, 2000GROUP
1625

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|------------------|-----|-----------------|------------|-------------|-------|-----------|-------------|
| BMR | AA1 | 5,281,619 | 01/25/1994 | Dell et al. | 514 | 454 | 03/22/1993 |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|------------------|-----|-----------------|------------|---------|-------|-----------|-------------|
| BMR | AL1 | EP 0 537 949 A1 | 04/21/1993 | Europe | — | — | Yes No |
| BMR | AM1 | EP 0 599 514 A2 | 06/01/1994 | Europe | — | — | Yes No |
| BMR | AN1 | EP 0 618 206 A1 | 10/05/1994 | Europe | — | — | Yes No |
| BMR | AO1 | EP 0 619 314 A1 | 10/12/1994 | Europe | — | — | Yes No |
| BMR | AP1 | WO 96/20721 | 07/11/1996 | WIPO | — | — | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|-----|----|---|--|
| BMR | AR | 1 | Al-Mousawi, S.M. et al., "Synthesis of New Condensed 2-Amino-4H-pyran-3-carbonitriles and of 2-Aminoquinoline-3-carbonitriles," <i>Organic Preparations and Procedures Int.</i> 31:305-313, Organic Preparations and Procedures Inc. (June 1999). |
| BMR | AS | 1 | Batteux, F. et al., "Gene Therapy of Experimental Autoimmune Thyroiditis by In Vivo Administration of Plasmid DNA Coding for Fas Ligand," <i>J. Immunol.</i> 162:603-608, The American Association of Immunologists (January 1999). |
| BMR | AT | 1 | Birch, K.A. et al., "LY290181, an Inhibitor of Diabetes-Induced Vascular Dysfunction, Blocks Protein Kinase C-Stimulated Transcriptional Activation Through Inhibition of Transcription Factor Binding to a Phorbol Response Element," <i>Diabetes</i> 45:642-650, The American Diabetes Association (1996). |

EXAMINER

Binta Johnson

DATE CONSIDERED

6/14/01

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

RECEIVED

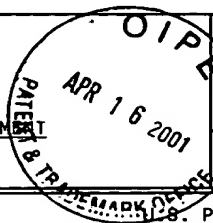
APR 17 2001

TECH CENTER 1600/2900

Page 2 of 9

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe et al.FILING DATE
November 6, 2000GROUP
1625

PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
| | AA | | | | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|-----|-----------------|------------|---------|-------|-----------|-------------|
| BMR | AL2 | WO 98/24427 | 06/11/1998 | WIPO | | | Yes No |
| BMR | AM2 | WO 99/18856 | 04/22/1999 | WIPO | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|-----|----|---|---|
| BMR | AR | 2 | Boirivant, M. et al., "Lamina Propria T Cells in Crohn's Disease and Other Gastrointestinal Inflammation Show Defective CD2 Pathway-Induced Apoptosis," <i>Gastroenterology</i> 116:557-565, American Gastroenterological Association (March 1999). |
| BMR | AS | 2 | Coven, T.R. et al., "PUVA-induced lymphocyte apoptosis: Mechanism of action in psoriasis," <i>Photodermatol. Photoimmunol. Photomed.</i> 15:22-27, Munksgaard (February 1999). |
| BMR | AT | 2 | Elagamey, A.G.A. et al., "Nitriles in Heterocyclic Synthesis: Novel Synthesis of Benzo[b]pyrans, Naphtho[1,2-b]pyrans, Naphtho[2,1-b]pyrans, Pyrano[3,2-h]quinolines and Pyrano[3,2-c]quinolines," <i>Collection Czechoslovak Chem. Commun.</i> 53:1534-1538, Institute of Organic Chemistry and Biochemistry (1988). |

EXAMINER

Bento Robinson

DATE CONSIDERED

6/9/01

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

RECEIVED

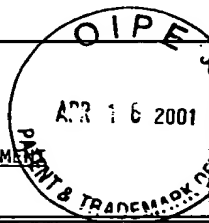
APR 17 2001

TECH CENTER 1600/2900

Page 3 of 9

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT


 PATTY. DOCKET NO.
 135.0410002/RWE/BEC

 APPLICATION NO.
 09/705,840

 APPLICANTS
 Grewe et al.

 FILING DATE
 November 6, 2000

 GROUP
 1625

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
| | AA | | | | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|-----|----|---|--|
| BMR | AR | 3 | Greenwald, R.B. et al., "Drug Delivery Systems Employing 1,4- or 1,6-Elimination: Poly(ethylene glycol) Prodrugs of Amine-Containing Compounds," J. Med. Chem. 42:3657-3667, American Chemical Society (September 1999) (Published on Web, August 13, 1999). |
| BMR | AS | 3 | Keenen, M. et al., "Methotrexate induces apoptotic cell death in human keratinocytes," Arch. Dermatol. Res. 290:240-245, Springer-Verlag (May 1998). |
| BMR | AT | 3 | Infante, A.J. et al., "The clinical spectrum in a large kindred with autoimmune lymphoproliferative syndrome caused by a Fas mutation that impairs lymphocyte apoptosis," J. Pediatr. 133:629-633, Mosby, Inc. (November 1998). |

EXAMINER

Binta Robinson

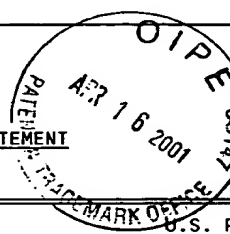
DATE CONSIDERED

6/14/9

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe et al.FILING DATE
November 6, 2000GROUP
1625

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|---|-------|-----------|-------------|
| | AA | | | RECEIVED APR 17 2001 TECH CENTER 1600/2900 | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|--|----|---|--|
| | AR | 4 | Klokot, G.V. et al., "Cyclization of Nitriles. XXIII. Addition of Active Phenols to Electron-deficient Ethylenes, Accompanied by Cyclization to 2-Amino-4H-benzo[b]pyrans. Crystal Structure of 2-Amino-4-(2-fluorophenyl)-3-ethoxycarbonyl-4H-naphtho[2,1-b]pyran," Zh. Org. Khim. 23:412-421, Nauka, Leningradskoe otdelenie (1987). |
| | AS | 4 | Klokot, G.V. et al., "Cyclization of Nitriles. XXIII. Addition of Active Phenols to Electron-deficient Ethylenes, Accompanied by Cyclization to 2-Amino-4H-benzo[b]pyrans. Crystal Structure of 2-Amino-4-(2-fluorophenyl)-3-ethoxycarbonyl-4H-naphtho[2,1-b]pyran," J. Org. Chem. USSR 23:369-377 (1987). |
| | AT | 4 | Leu, Y.-L. et al., "Design and Synthesis of Water-Soluble Glucuronide Derivatives of Camptothecin for Cancer Prodrug Monotherapy and Antibody-Directed Enzyme Prodrug Therapy (ADEPT)," J. Med. Chem. 42:3623-3628, American Chemical Society (September 1999) (Published on Web, August 24, 1999). |

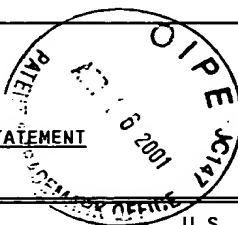
EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe *et al.*FILING DATE
November 6, 2000GROUP
1625

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
| | AA | | | | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|--|----|---|---|
| | AR | 5 | López-Hoyos, M. <i>et al.</i> , "Regulation of B cell apoptosis by Bcl-2 and Bcl-X _L and its role in the development of autoimmune diseases (Review)," <i>Int. J. Mol. Med.</i> 1:475-483 (February 1998). |
| | AS | 5 | O'Reilly, L.A. and Strasser, A., "Apoptosis and autoimmune disease," <i>Inflamm. Res.</i> 48:5-21, Birkhäuser Verlag (January 1999). |
| | AT | 5 | Ohsako, S. and Elkon, K.B., "Apoptosis in the effector phase of autoimmune diabetes, multiple sclerosis and thyroiditis," <i>Cell Death Differ.</i> 6:13-21, Stockton Press (January 1999). |

EXAMINER

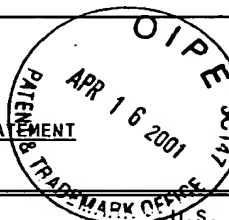
DATE CONSIDERED

6/4/01

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe et al.FILING DATE
November 6, 2000GROUP
1625

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
| | AA | | | | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

RECEIVED

APR 17 2001

TECH CENTER 1600/2900

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|------------|----|----------|---|
| <i>BMR</i> | AR | <u>6</u> | Ozawa, M. et al., "312-nanometer Ultraviolet B Light (Narrow-Band UVB) Induces Apoptosis of T Cells within Psoriatic Lesions," <i>J. Exp. Med.</i> 189:711-718, The Rockefeller University Press (February 1999). |
| <i>BMR</i> | AS | <u>6</u> | Panda, D. et al., "Suppression of Microtubule Dynamics by LY290181. A Potential Mechanism for its Antiproliferative Action," <i>J. Biol. Chem.</i> 272:7681-7687, The American Society for Biochemistry and Molecular Biology, Inc. (1997). |
| <i>BMR</i> | AT | <u>6</u> | Radwan, S.M. et al., "Synthesis and Some Reactions of New Benzo[b]pyran Derivatives," <i>Phosphorus, Sulfur, and Silicon</i> 101:207-211, Gordon and Breach Publishers (1995). |

EXAMINER

Bento Robinson

DATE CONSIDERED

6/4/0

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

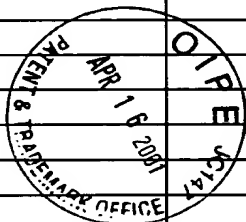
FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe et al.FILING DATE
November 6, 2000GROUP
1625

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
| | AA | | | | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |



RECEIVED

APR 17 2001

TECH CENTER 1600/2900

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|------------|----|---|---|
| <i>BMR</i> | AR | Z | Savill, J., "Apoptosis in resolution of inflammation," <i>J. Leukoc. Biol.</i> 61:375-380, Society for Leukocyte Biology (1997). |
| <i>BMR</i> | AS | Z | Sharanin, Yu.A. and Klokot, G.V., "Synthesis of 2-Amino-4H-chromenes," <i>Zh. Org. Khim.</i> 19:1782-1784, Nauka, Leningradskoe otdelenie (1983). |
| <i>BMR</i> | AT | Z | Sharanin, Yu.A. and Klokot, G.V., "Synthesis of 2-Amino-4H-chromenes," <i>J. Org. Chem. USSR</i> 19:1582-1583 (1983). |

EXAMINER

Binta Robinson

DATE CONSIDERED

6/4/01

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe *et al.*FILING DATE
November 6, 2000GROUP
1625

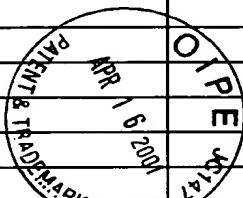
U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
| | AA | | | | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

RECEIVED

APR 17 2001

TECH CENTER 1600/2900



FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|--|----|---|--|
| | AR | 8 | Smith, C.W. <i>et al.</i> , "The Anti-rheumatic Potential of a Series of 2,4-Di-substituted-4H-naphtho[1,2-b]pyran-3-carbonitriles," <i>Bioorg. Med. Chem. Lett.</i> 5:2783-2788, Elsevier Science Ltd. (1995). |
| | AS | 8 | Vaishnav, A.K. <i>et al.</i> , "The molecular basis for apoptotic defects in patients with CD95 (Fas/Apo-1) mutations," <i>J. Clin. Invest.</i> 103:355-363, American Society for Clinical Investigation (February 1999). |
| | AT | 8 | Wakisaka, S. <i>et al.</i> , "Modulation by proinflammatory cytokines of Fas/Fas ligand-mediated apoptotic cell death of synovial cells in patients with rheumatoid arthritis (RA)," <i>Clin. Exp. Immunol.</i> 114:119-128, Blackwell Science (October 1998). |

EXAMINER

DATE CONSIDERED

6/4/01

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1735.0410002/RWE/BECAPPLICATION NO.
09/705,840APPLICANTS
Drewe et al.FILING DATE
November 6, 2000GROUP
1625

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
| | AA | | | | | | |
| | AB | | | | | | |
| | AC | | | | | | |
| | AD | | | | | | |
| | AE | | | | | | |
| | AF | | | | | | |
| | AG | | | | | | |
| | AH | | | | | | |
| | AI | | | | | | |
| | AJ | | | | | | |
| | AK | | | | | | |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

| | | | |
|--|----|---|---|
| | AR | 2 | Wood, D.L. et al., "Inhibition of Mitosis and Microtubule Function through Direct Tubulin Binding by a Novel Antiproliferative Naphthopyran LY290181," <i>Mol. Pharmacol.</i> 52:437-444, The American Society for Pharmacology and Experimental Therapeutics (1997). |
| | AS | 2 | Zhou, T. et al., "Bisindolylmaleimide VIII facilitates Fas-mediated apoptosis and inhibits T cell-mediated autoimmune diseases," <i>Nat. Med.</i> 5:42-48, Nature Publishing Group (January 1999). |
| | AT | | |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.